Neighborhood Socioeconomic Disadvantage and the Neurobiology of Uncertainty in Traumatically Injured Adults

Supplement

Supplemental Methods

MRI acquisition

All imaging was collected on a General Electric Discovery MR750 3.0 Tesla scanner with a 32-channel head-coil (Waukesha, WI). A T1-weighted high-resolution anatomical scan was acquired for coregistration with the functional data and used the following parameters: FOV = 240mm; matrix = 256 x 224; slice thickness = 1mm; 150 slices; repetition time (TR)/ echo time (TE) = 8.2/3.2; flip angle = 12°, voxel size = 0.9375 x 1.071 x 1. Functional T_2*-weighted echoplanar images (EPI) were acquired with the following parameters: FOV = 22.4mm; matrix = 64 x 64; slice thickness = 3.5mm; 41 sagittal slices; TR/TE = 2000/25ms; flip angle = 77°. Each of the 4 runs was approximately 246 seconds (123 images).

fMRI Preprocessing and Analysis

Task-based fMRI data was analyzed using Analysis of Functional Neuroimages (AFNI) software (Cox, 1996). The first 3 volumes were removed and EPI data was slice-time corrected. Images were spatially smoothed (full-width-half-maximum = 4mm) and transformed to Montreal Neurological Institute space (MNI 152; McGill University, Montreal, Quebec). Head movements were corrected using a six-parameter (rigid body) linear transformation followed by a nonlinear transformation, with the minimum outlying volume as reference. EPI data was scaled to percent signal change. Volumes with excessive motion (Euclidian norm > .3mm), outlying TRs (> 10% outlying voxels), and head motion parameters were regressed out to improve signal-to-noise ratio. Individuals were removed from analysis if more than 20% of TRs were censored (44 subjects).

Picture Anticipation Task

Stimuli were presented using E-Prime 2.0 (Psychology Software Tools, Pittsburgh, PA) interfaced with an MRI compatible response box to record key presses. To keep subjects attending to the trials, subjects were asked to determine if the image was indoors or outdoors with a button press. All trials were included in fMRI analysis because accuracy across all conditions was acceptable (Overall $M_{accuracy} = 75.5$). We hypothesize trial accuracy was considerably lower than noted in Somerville et al., (2013) due to the trauma-related nature of the negative images.

There were 104 total images in the task (52 negative, 52 neutral; 26 per condition). Half of the images were from the International Affective Picture Set (Bradley & Lang, 2007) and half from the Nencki Affective Picture System (Marchewka et al., 2014). Half of the images took place indoors and half outdoors. Stimuli were matched for number of images displaying people and images showing visible faces. The neutral images from the two picture sets were matched for valence (NAPS: $M = 5.4$, $SD = .57$; IAPS: $M = 5.42$, $SD = .47$) and arousal (NAPS: $M = 4.81$, $SD = .47$; IAPS: $M = 3.51$, $SD = .56$). The negative images were also matched for valence (NAPS: $M = 2.09$, $SD = .35$; IAPS: $M = 2.04$, $SD = .38$) and arousal (NAPS: $M = 7.28$, $SD = .41$; IAPS: $M = 6.33$, $SD = .64$).

Subjective Ratings of Anxiety

At the end of each block of trials, participants completed a brief subjective rating to assess their level of anxiety associated with the block. They were asked to rate their anxiety on a scale from 1 “not at all anxious” to 9 “very anxious”: “How anxious did you feel during the (first, second) set of trials in the previous run, which had (predictable, unpredictable) timings and (negative, neutral) images?" These subjective ratings were used as a manipulation check to determine if the anticipation and exposure to negative images elicited more anxiety than that of the neutral images, and to evaluate anxiety between predictable and unpredictable blocks of trials.

Supplemental Results

Without PTSD symptom covariates

To evaluate activation related to ADI without adjusting for acute PTSD symptom severity, we repeated the analyses in the main text but removed the PCL (income, gender, and age still served as covariates). Findings overlapped with those reported in the main text for both the stimulus anticipation (Supplemental Table S1) and stimulus presentation (Supplemental Table S2) periods.

There was one notable difference in the ADI results compared to the main analysis during the stimulus presentation period. Greater ADI rankings were related to positive activation of the anterior insula to predictable neutral images and negative activation of the anterior insula to unpredictable neutral images. Insula activation in the face of unpredictability is frequently observed; however, the majority of studies (e.g. Gorka et al., 2016; Shankman et al., 2014) report insula hyperactivation to uncertain conditions. Interestingly, we found greater neighborhood disadvantage is associated with the contrary. In the context of the results presented in the main analysis, this further supports the association of neighborhood disadvantage with dysregulated uncertainty processing.

Supplemental Table S1.
Coordinates of peak whole brain activation by task condition during stimulus **anticipation period** *without controlling for PCL*

Task Condition	***Brain Region***	***X***	***Y***	***Z***	***k***	***Z***
Neu > Neg	Right middle temporal gyrus	45	-67	0	22	3.86
P > U	Left middle occipital gyrus	-46	-71	0	41	4.97
	Right superior occipital gyrus	17	-88	32	24	3.42
	Right superior parietal lobule	35	-53	60	15	4.77
Uneu > Uneg	Bilateral middle cingulate cortex	0	-32	46	27	3.87
Uneu > Pneu	Bilateral middle occipital gyrus	0	-25	39	28	4.51
Pneu > Uneu	Left middle occipital gyrus	45	70	0	22	5.17
Pneu > Uneu & ADI	Right anterior cingulate cortex	7	27	25	16	3.69
Uneu & ADI	Left parahippocampal gyrus	-18	-32	-21	24	-3.30
	Left piriform cortex	-21	6	-17	15	-3.46
Pneg & ADI	Left middle occipital gyrus	-39	-81	0	41	-5.25
	Right inferior occipital gyrus	31	-92	-7	22	-4.47
Pneu & ADI	Right hippocampus	21	-32	-3	26	3.46

Abbreviations: **U**, unpredictable; **P**, predictable; **Neg**, negative; **Neu**, neutral; **ADI**, area deprivation index; **XYZ**, peak coordinates in standard space (MNI152); **k**, cluster size; **Z**, z-score. *Note:* For results with ADI, gender, age, and income were included as covariates in the model. Cluster thresholds: voxel wise: $p < 0.001$, cluster wise $k > 14$, $p < 0.05$.

Supplemental Table S2.
Coordinates of peak whole brain activation by task condition during **stimulus presentation** *without controlling for PCL*

Task Condition	***Brain Region***	***X***	***Y***	***Z***	***k***	***Z***
Neg > Neu	Right fusiform gyrus	35	-78	-14	1531	7.50
	Left fusiform gyrus	-35	81	-17	1422	7.13
	Right precentral gyrus	42	6	28	525	7.24
	Bilateral cerebellum	0	-57	-38	210	6.81
	Left precentral gyrus	-42	3	35	129	6.79
	Left hippocampus	-25	-29	-3	60	6.86
	Left amygdala	-21	-1	-14	26	4.04
	Left inferior frontal gyrus	-49	38	11	24	4.76
	Right thalamus	21	-32	4	18	4.66
	Bilateral superior colliculi	3	-32	-3	16	3.45
Uneg > Uneu	Right inferior occipital gyrus	31	-81	-14	660	5.09
	Left inferior occipital gyrus	-39	-71	-17	378	4.84
	Right precentral gyrus	42	6	32	149	5.34
	Left middle occipital gyrus	-28	-74	25	70	4.24
	Left precentral gyrus	-42	3	28	34	5.54
	Right precentral gyrus	38	-1	49	14	5.17
Pneg > Pneu	Right fusiform gyrus	35	-78	-14	1014	5.66
	Left fusiform gyrus	-35	-81	-17	938	5.58
	Right precentral gyrus	42	6	28	210	5.79
	Bilateral cerebellum	0	-57	-38	144	6.01
	Left precentral gyrus	-45	3	35	53	4.72
	Left hippocampus	-21	-29	-3	50	4.14
	Right inferior frontal gyrus	49	38	11	34	4.60
	Left inferior frontal gyrus	-49	41	11	18	3.32
Uneg & ADI	Left inferior temporal gyrus	-49	-43	-17	24	-3.92
Uneu & ADI	Left parahippocampal gyrus	-18	-36	-21	21	-3.30
	Left anterior insula	-35	10	-14	14	-3.30
Pneg & ADI	Right inferior frontal gyrus	42	34	11	82	-5.22
	Left anterior cingulate cortex	-14	45	-3	39	-3.55
	Right superior frontal gyrus	21	34	42	16	-5.04
	Left inferior temporal gyrus	-46	-39	-17	14	-3.37
Pneu & ADI	Left middle temporal gyrus	-56	-64	21	81	-3.35
	Left posterior cingulate cortex	0	-43	32	77	-3.60
	Left superior frontal gyrus	-21	66	4	51	-3.44
	Left calcarine gyrus	-14	-60	11	21	-3.56
	Right anterior insula	38	17	-7	19	3.31
	Left precentral gyrus	-39	-11	56	14	-3.59

Abbreviations: **U**, unpredictable; **P**, predictable; **Neg**, negative; **Neu**, neutral; **ADI**, area deprivation index; **XYZ**, peak coordinates in standard space (MNI152); **k**, cluster size; **Z**, z-score. *Note:* For results with ADI, gender, age, and income were included as covariates in the model. Cluster thresholds: voxel wise: $p < 0.001$, cluster wise $k > 14$, $p < 0.05$.

Sensitivity Analysis

To determine whether the results of the main analysis were driven by individuals living in the most disadvantaged neighborhoods (Bell et al., 2021; Webb et al., 2021), we excluded participants with ADI rankings greater than 90 (N = 17) and reran all analyses (N = 73). Results showed the same general pattern as those with the full sample (reported in the main text) during both the stimulus anticipation (Supplemental Table S3) and stimulus presentation periods (Supplemental Table S4), suggesting results were not driven by individuals living in the most disadvantaged contexts.

Supplemental Table S3.
Coordinates of peak whole brain activation by task condition during stimulus **anticipation period**

Task Condition	***Brain Region***	***X***	***Y***	***Z***	***k***	***Z***
P > U	Left middle occipital gyrus	-45	-70	0	68	5.23
	Right superior parietal lobule	21	-67	63	41	5.02
	Left superior parietal lobule	-21	-70	67	30	3.50
	Right middle occipital gyrus	31	-91	4	23	4.25
	Right middle occipital gyrus	28	-77	28	22	4.15
Uneu > Uneg	Right middle cingulate cortex	3.5	-35	49	20	3.50
	Right middle cingulate cortex	7	-14	46	14	4.00
Pneg > Uneg	Right calcarine gyrus	7	-84	11	52	4.06
Pneu > Uneu	Left middle occipital gyrus	-45	-70	0	46	5.55
Pneu > Pneg & ADI	Left cerebellum	-17	-67	-27	17	5.60
	Right primary motor cortex	45	0	32	15	4.43
Pneu > Uneu & ADI	Right posterior cingulate cortex	14	-53	32	70	3.98
Pneg & ADI	Left middle occipital gyrus	-38	-81	0	69	-4.48
	Right primary motor cortex	45	0	32	22	-4.98
	Left cerebellum	-31	-81	-38	16	-3.35
	Right fusiform gyrus	28	-88	-3	15	-3.53
	Left middle temporal gyrus	-45	-53	-3	15	-4.60
Pneu & ADI	Right posterior cingulate cortex	3.5	-60	21	59	4.31

Abbreviations: **U**, unpredictable; **P**, predictable; **Neg**, negative; **Neu**, neutral; **ADI**, area deprivation index; **XYZ**, peak coordinates in standard space (MNI152); **k**, cluster size; **Z**, z-score. *Note:* For results with ADI, gender, age, PCL-5, and income were included as covariates in the model. Cluster thresholds: voxel wise: $p < 0.001$, cluster wise $k > 14$, $p < 0.05$.

Supplemental Table S4.
Coordinates of peak whole brain activation by task condition during **stimulus presentation**

Task Condition	***Brain Region***	***X***	***Y***	***Z***	***k***	***Z***
P > U	Left lingual gyrus	-7	91	-6	32	4.77
Neg > Neu	Bilateral inferior occipital gyrus	31	-81	-13	6499	10.73
	Bilateral inferior frontal gyrus	38	6	32	3178	6.45
	Right amygdala	24	-1	-17	206	6.46
	Right cerebellum	14	-50	-49	29	5.59
	Right inferior temporal gyrus	45	3	-45	27	4.64
	Left cerebellum	-49	-67	-42	14	4.17
Uneg > Uneu	Right inferior occipital gyrus	31	-81	-14	1640	7.78
	Left inferior occipital gyrus	-35	-78	-17	1323	5.83
	Right inferior frontal gyrus	45	6	25	277	5.34
	Bilateral cerebellum	0	-57	-38	110	4.47
	Left precentral gyrus	-42	3	32	94	4.60
	Right inferior frontal gyrus	49	41	14	32	4.82
	Left inferior parietal lobule	-49	-57	49	24	5.03
	Right amygdala	21	-1	-14	22	5.13
	Left cingulate gyrus	-24	-50	21	15	3.66
	Left middle frontal gyrus	-46	24	39	14	4.34
Pneg > Pneu	Bilateral inferior occipital gyrus	31	-81	-14	3636	7.34
	Right inferior frontal gyrus	38	6	32	1103	5.49
	Left inferior frontal gyrus	-42	3	35	148	5.35
	Right hippocampus	24	-29	-3	103	5.88
	Left inferior frontal gyrus	-49	38	11	48	3.89
	Left hippocampus	-25	-29	-3	42	5.55
	Right middle cingulate gyrus	21	-1	18	25	4.02
	Right cerebellum	10	-81	-42	24	4.67
	Left amygdala	-21	-4	-14	23	4.63
	Right fusiform gyrus	42	-15	-28	15	5.08
Pneg > Uneg	Right superior occipital gyrus	17	-95	18	44	3.89
Neu > Neg & ADI	Left inferior temporal gyrus	-49	-43	-17	61	3.9
	Right middle temporal gyrus	49	-56	-3	22	3.67
P > U & ADI	Right precuneus	3	-46	46	31	4.56
Pneu > Uneu & ADI	Right middle cingulate cortex	10	-39	42	24	4.19
Uneg & ADI	Left fusiform gyrus	-38	-50	-17	87	-4.42
	Left calcarine gyrus	-21	-60	7	45	-4.30
	Right angular gyrus	45	-57	42	39	-4.16
	Right precuneus	7	-57	46	22	-4.11
	Left inferior parietal lobule	-49	-57	46	17	-3.95
	Right fusiform gyrus	42	-57	-14	14	-4.15
Pneg & ADI	Left inferior temporal gyrus	-46	-39	-17	32	-4.02
	Left precuneus	-7	-57	70	15	-3.66

Abbreviations: **U**, unpredictable; **P**, predictable; **Neg**, negative; **Neu**, neutral; **ADI**, area deprivation index; **XYZ**, peak coordinates in standard space (MNI152); **k**, cluster size; **Z**, z-score. *Note:* For results with ADI, gender, age, PCL-5, and income were included as covariates in the model. Cluster thresholds: voxel wise: $p < 0.001$, cluster wise $k > 14$, $p < 0.05$.

Supplemental References

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